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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,883	05/14/2001	Lex M. Cowsert	ISPH-0576	9012

36441 7590 02/17/2004

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EXAMINER
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ZARA, JANE J

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 02/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/854,883

Applicant(s)

COWSERT ET AL.

Examiner

Jane Zara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 26 November 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,4-20,22,25,26,29-32,37,38 and 41-50 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 22,25,26,29-32,41-47 and 49 is/are allowed.
- 6) ☒ Claim(s) 1,2,4-20,37,38,48 and 50 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

This Office action is in response to the communication filed 11-26-03.

Claims 1,2,4-20,22,25,26,29-32,37,38 and 41-50 are pending in the instant application.

#### ***Response to Arguments and Amendments***

##### **Withdrawn Rejections**

Any rejections not repeated in this Office action are hereby withdrawn.

##### **Maintained Rejections**

Claims 37 and 38 are rejected under 35 U.S.C. 112, first paragraph, for lacking enablement over the scope claimed, for the reasons of record set forth in the Office actions mailed November 5, 2002 and June 7, 2003.

No new arguments have been presented addressing this rejection.

Claims 1, 2, 4-20, 48 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Huang et al, Olefsky, Chernoff et al, Milner et al and Baracchini et al for the reasons of record set forth in the Office action mailed June 7, 2003.

Applicant's arguments filed 11-26-03 have been fully considered but they are not persuasive. Applicants argue that the instant obviousness rejection is improper for several reasons. Applicants argue that Huang fails to identify the sequence of the antisense oligonucleotide that was used to inhibit the target PTP1B in rat cells in vitro

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and therefore it cannot be determined whether this antisense oligonucleotide used for inhibition of PTP1B in rat cells would indeed inhibit the target human PTP1B of SEQ ID NO: 243, nor to what extent inhibition would occur. Contrary to Applicants' assertions concerning the improper reliance upon Huang for the instant 103 rejection, Huang properly provides a motivation for inhibiting the target gene PTP1B (to determine its involvement in modulating tyrosine phosphorylation of specific proteins and, hence its effect(s) on related cellular processes) and a means for inhibiting the target gene PTP1B of known nucleic acid sequence using antisense. The fact that Huang does not specifically inhibit the expression of human PTP1B of SEQ ID NO: 243 does not negate its validity as an appropriate reference for a proper obviousness rejection.

Applicants also argue that Olefsky is improperly cited in the 103 rejection of record because it does not teach specific antisense sequences that target and inhibit the expression of human PTP1B. Contrary to Applicants' assertion, Olefsky is relied upon in the instant 103 rejection because it teaches the association between PTP1B and insulin receptor activation, implicating PTP1B as a "key target in insulin receptor signal transduction." (See col. 1, lines 33-39) Olefsky therefore provides the motivation to inhibit PTP1B expression in an organism as "a method of treating insulin resistance associated disorders in a patient." (See col. 1, lines 33-39) In addition, Olefsky teaches the use of antisense nucleic acid for interfering with the translation of mRNA encoding human PTP1B, indicating that antisense technology is widely used for inhibiting the expression of a known target gene (See col. 5, lines 23-36). If Huang and Olefsky had taught what Applicants argue that they didn't teach (e.g. the targeting and inhibition of

SEQ ID NO: 243), they would in fact anticipate, not merely render obvious (as indeed they have), the instantly claimed invention.

Applicants argue further that Chernoff merely discloses the nucleotide sequence of SEQ ID NO: 243, but fails to teach or suggest any specific sequences for antisense compounds to bind and inhibit expression of SEQ ID NO: 243, and therefore does not add anything to the primary references in combination with the secondary references to properly render the instantly claimed invention obvious. Contrary to Applicants' assertions, the disclosure by Chernoff of the nucleotide sequence of human PTP1B of SEQ ID NO: 243, combined with the motivation(s) provided by Huang and Olefsky for targeting and inhibiting the expression of PTP1B, provides ample motivation and proper means to target and inhibit the expression of SEQ ID NO: 243 in vitro. Furthermore, the reliance upon Milner to teach the now routine experimentation of designing and assessing various antisense oligonucleotides to specifically bind and inhibit the expression of a target gene of known nucleotide sequence in vitro - combined with the teachings of Chernoff, Huang and Olefsky - together provide ample means and motivation to render the instant invention obvious to one of ordinary skill in the art. One of ordinary skill in the art would have a reasonable expectation of success using the disclosures of Chernoff and Milner to design, test and identify antisense oligonucleotides (including between 8-50 nucleobases in length) for their ability to inhibit the expression of SEQ ID NO: 243 by at least 50% in vitro. Therefore, the instant 103 rejection is properly maintained.

Applicants argue that Baracchini is not appropriate because it only generally teaches various modifications that are incorporated into antisense oligonucleotides. Contrary to Applicants' assertions, Baracchini is properly cited because it teaches the general applicability of incorporating the claimed modifications into antisense oligonucleotides. These modifications do not depend on a particular oligonucleotide sequence, and the modifications incorporated into an antisense that targets MRP can also be used in an antisense that targets PTP1B. Therefore, the instant 103 rejection is maintained.

***Allowable Subject Matter***

Claims 22, 25, 26, 29-32, 41-47 and 49 appear free of the prior art.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

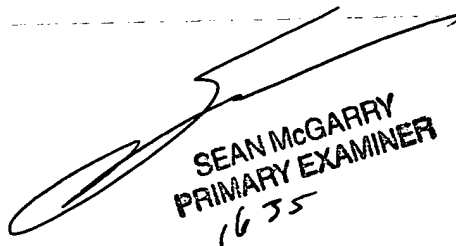
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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765**. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

**JZ**  
February 1, 2004

  
SEAN MCGARRY  
PRIMARY EXAMINER  
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